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| 09/913,728      | 10/23/2001  | Toshio Kitamura      | 084335-0143         | 3800             |

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EXAMINER

DEBERRY, REGINA M

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1647

DATE MAILED: 11/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/913,728

Applicant(s)

KITAMURA ET AL.

Examiner

Regina M. DeBerry

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) 6,10-12 and 25-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-9 and 13-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

***Status of Application, Amendments and/or Claims***

The amendment filed 27 August 2003 has been entered in part. New claims 13-32 were added, however claims 25-32 will not be examined because these newly submitted claims are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 25-32 are drawn to non-elected SEQ ID NOs. Please see Restriction/Election requirement 08 November 2002.

Since Applicants have received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-32 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 1-5, 7-9 and 13-24 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The specification is now in compliance with 37 CFR 1.821-1.825 of the Sequence Rules and Regulations.

The Examiner will re-send the initialed PTO 1449 from the previously filed IDS.

***Withdrawn Objections And/Or Rejections***

The objection to claims 1, 5 and 8 as set forth at page 2 of the previous Office Action (27 February 2003) is *withdrawn* in view of the amendment (27 August 2003).

The rejection of claims 1 and 4 under 35 USC 101 for being directed to non-statutory subject matter as set forth at pages 3-4 of the previous Office Action

(27 February 2003) is *withdrawn* in view of the amendment (27 August 2003).

The rejection of claims 1, 4 and 7 under 35 U.S.C. 102(b) as being anticipated by Noguchi *et al.* (Blood 78:2548-2556, 1991, IDS A7, Paper No. 9) as set forth at pages 11-12 of the previous Office Action (27 February 2003) is *withdrawn* in view of the amendment (27 August 2003).

### **Disclosure Objection**

The amendment filed 27 August 2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "1 to 30 amino acids substituted, deleted....", "1 to 15 amino acids substituted, deleted.....", "1 to 5 amino acids substituted, deleted..." and "washing condition of 1.0x SSCP, 0.1% SDS at 65°C". Applicant is required to cancel the new matter in the reply to this Office Action.

### **Claim Rejections - 35 USC § 112, First Paragraph, Written Description, New Matter**

Claims 1c, 2-7, 9, 13-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.** The specification as originally filed does not provide support for the invention as now

claimed: "1 to 30 amino acids substituted, deleted...." (claim 1c), "1 to 15 amino acids substituted, deleted....." (claims 13, 18), "1 to 5 amino acids substituted, deleted..." (claims 14, 19) and "washing condition of 1.0x SSCP, 0.1% SDS at 65°C" (claims 17, 22).

Applicants' amendment, filed 27 August 2003, asserts that no new matter has been added but does not provide sufficient direction for the written description for the above-mentioned "limitations".

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations". The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. Applicants are required to cancel the new matter in the response to this Office action. Alternatively, Applicants are invited to provide specific written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

#### **Claim Rejections - 35 USC § 102(b)**

Claim 8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Noguchi *et al.* (Blood 78:2548-2556, 1991, IDS A7, Paper No. 9). The basis for this rejection is set forth at pages 11-12 of the previous Office Action (27 February 2003). Applicants state that Noguchi *et al.* do not describe a DNA encoding a protein consisting of an amino acid sequence with 70% or higher homology to SEQ ID NO:2. Applicants submit a BLASTP analysis. Applicants maintain that the homology between the protein of the

invention (Delta1) and the protein of Noguchi *et al.* (erythropoietin receptor) is not 70% or higher homology to SEQ ID NO:2.

Applicants' arguments have been fully considered but not deemed persuasive for the following reasons. The instant claim recites a nucleotide that hybridizes with a DNA consisting of a nucleotide of SEQ ID NO:1 or a complementary strand thereof, having a chain length of at least 15 bases. The instant claim *does not* recite a DNA encoding a protein consisting of an amino acid sequence with 70% or higher homology to SEQ ID NO:2. Furthermore, in the absence of a recitation of clear hybridization conditions, any polynucleotide sequence will hybridize to SEQ ID NO:1. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

#### **Claim Rejections - 35 USC § 101**

Claims 7, 8, 23 and 24 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The instant claims as they stand are not limited to isolated and purified polypeptides and/or polynucleotides and encompass the full length naturally occurring product and therefore reads on products of nature.

Claims 1-5, 7-9, 13-24 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The basis for this rejection is set forth at pages 3-7 of the previous Office Action (27 February 2003).

Applicants state that the Examiner admits that the specification teaches the amino acid sequence encoding Delta1 as a novel cytokine receptor. Applicants cite the specification as teaching where the gene was cloned and is expressed. Applicants state that the membrane proximal region of human EPOR can be replaced with that region from the inventive protein and the engineered protein can activate JAK2. Applicants maintain that Delta1 can be a tissue-specific marker because the transcript has been identified in tissues such as heart, brain, lung, and kidney but not skeletal or muscle. Applicants add that Delta1 can be a genetic marker because the precise location of Delta1 has been determined.

Applicants' arguments have been fully considered but not deemed persuasive for the following reasons. The Examiner was merely stating the information recited in the specification. The fact that the proximal region of human EPO receptor can be replaced with that region from the Delta1 and that the engineered protein can activate JAK2 in response to EPO is questionable because the chimera comprising the extracellular region of hEPOR/cytoplasmic region of Delta1 was inactive (Figure 5 and Figure 6). Most importantly, the specification never discloses a true ligand of Delta1. Thus it would be unclear how to activate and/or inhibit this protein and therefore how to use it. A tissue-specific marker or genetic marker is not specific and substantial utilities for Delta1. There are many genes that are expressed in the heart, brain, lung that are not expressed in muscle or skeletal; many genes have been mapped to a specific chromosomal location. A specific utility is a utility that is specific to the subject matter claimed. A claimed DNA that hybridizes near a disease-associated gene or it has a

gene regulating activity would be a practical use of the material. However, the chromosomal location of a gene that has no particular correlation with a disease or gene regulating activity would not constitute a substantial utility.

Lastly, Applicants contend that the ligand of the protein of the invention is the thymic stromal lymphoprotein (TSLP), which facilitates B lymphopoiesis and stimulates thymocytes and mature T cells. Applicants submit Pandey *et al.*, Nature Immunol, 2000 and Parks *et al.* J. Exp. Medicine, 2000.

Applicants' arguments have been fully considered but not deemed persuasive for the following reasons. Applicants fail to submit a sequence comparison between Delta1 and the receptor protein of Pandey *et al.* and Parks *et al.* For that reason it is not clear if Delta1 and the receptor protein of Pandey and Parks are the same. **Most importantly**, the Pandey and Parks references teach that TSLP receptor *cooperates with IL-7 $\alpha$  receptor* to mediate signaling in response to TSLP. Thus the IL-7 $\alpha$  receptor is obligatory for the signaling complex (Pandey *et al.*, abstract and Discussion, page 63; Park *et al.*, abstract and Discussion, page 667-668). The specification as originally filed does not have support for TSLP ligand or IL-7 $\alpha$  receptor. Therefore, the specification *as originally filed* lacks a specific and substantial asserted utility or a well established utility. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

**Claim Rejections - 35 USC § 112, First Paragraph, Enablement**

Claims 1-5, 7-9, 13-24 remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at pages 7-9 of the previous Office Action (27 February 2003).

Applicants incorporate their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicants' arguments have been fully considered but are not found to persuasive for the reasons discussed above in the maintained rejection in 35 USC 101.

Applicants assert that the PTO's explanation must further include specific technical reasons that cast doubt on the claim's enablement. Applicants state that the PTO never cited sufficient evidence to support its assertions. Applicants maintain that the present invention discloses methods for making variants of the instant invention. Applicants cite pages in the specification. Applicants state that the specification provides a means for assaying activity of a mutant or variant protein of the inventive protein, as indicated by the ability to activate JAK2.

Applicants' arguments have been fully considered but are not found persuasive. Even if an assay was provided to discern JAK2 activity, the specification would not support claims to polynucleotides encoding Delta1 polypeptides modified to an unlimited extent relative to those exemplified. Wells, Biochemistry 29:8509-8517, 1990 was cited

by the Examiner to show that certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. The specification states that these types of changes are routinely done in the art and provides a list of potential amino acid substitutions. The specification, however, does not provide any guidance as to *what* changes should be made and *which* regions of the instant protein are functionally and structurally critical. There is no description of variants of SEQ ID NO:2 that exist, while still maintaining function. Furthermore, claim 5 does not specify that the protein produced by that of SEQ ID NO:2 and therefore any produced by the "host cell" is conceivably encompassed. Specific, not general guidance is what is needed. For the reasons discussed above, such experimentation would be undue for one skilled in this art. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

#### **Claim Rejections - 35 USC § 112, First Paragraph, Written Description**

Claims 1, 5, 7, 8 and 13-24 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pages 9-11 of the previous Office Action (27 February 2003).

Applicants state that the present versions of the claims are believed to avoid the concerns addressed in the Office Action. Applicants state that the specification discloses specific hybridization conditions for isolating DNA encoding a functionally equivalent protein of the present invention. Applicants state that the specification discloses that a gene encoding a functionally equivalent protein may be identified by PCR using a portion of the DNA encoding the protein as a primer. Applicants maintain that the specification discloses at least two independent methods for obtaining a functionally equivalent protein of the present invention. Applicants conclude, that the specification indicates significant cross-hybridization does not occur with DNAs encoding other proteins under normal hybridization conditions, preferably under stringent hybridization conditions.

Applicants' arguments have been fully considered but not deemed persuasive. The Examiner will not address the hybridization arguments because the newly submitted claims, except for claim 8, have been amended to recite hybridization language. As was stated in the last Office Action, one cannot describe what one has not conceived. Applicants assert that the functionally equivalent proteins can be obtained via gene amplification. However, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. As was stated about, claim 5 encompasses any protein produced by the host cell. The specification discloses only a structural feature of SEQ ID NO:1. The claims encompass genes yet to be discovered. There is no disclosure regarding the coding capacity of any of the variants cited.. Defining the fragment in functional terms

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would not suffice in the absence of a disclosure of structural features or elements of a cDNA that would encode a protein having a stated function. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

### **Claim Objections**

Claim 8 is objected to because a nucleotide is a base, a sugar and a phosphate. Nucleotides themselves cannot, by definition, at least 15 bases, they have one base. Appropriate correction is required.

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

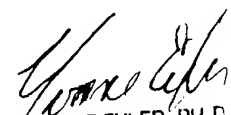
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



RMD

November 17, 2003



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